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A pilot study to identify barriers to treatment in OIF/OEF veterans with PTSD and low back pain in establishing transdisciplinary complementary interventions

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14. ABSTRACT The purpose of the proposed research is to empirically explore the effectiveness of standard clinical intervention for Veterans with CLBP and PTSD given multiple medical and psychiatric comorbidities, particularly in OEF/OIF Veterans. A total of 318 Veteran charts from Back School Log over 18 months were examined and divided into four Groups based on the diagnosis of PTSD and OEF/OIF status. The mean overall age was 55.86 yrs (SD 13.88) with a significant difference ($p<.001$), between Non OEF/OIF Groups 1&2 (59.34 yrs, SD11.4) and OEF/OIF Groups 3&4 (35.24 yrs, SD 8.08). While males were the overall majority (95.6%), a significant number of females constituted the OEF/OIF Groups 3&4, (20%, $p<.0001$). Further, a significantly higher percentage of OEF/OIF Veterans were exposed to combat (34.8%, $p=.02$). The majority of those with PTSD were from the Army (65.28%, $p=.0026$). There was no difference among groups with race or marital status. The majority of Veterans completed Back School I with an average VNS 4.9 with a significantly greater improvement ($p=.0024$) in those without PTSD. Those who continued on to Back School II demonstrated a significant difference ($p=.05$) with only a 50% completion rate in OEF/OIF Veterans with PTSD. Overall, those with a diagnosis of PTSD reported lower improvements in functional activities, i.e. sitting and walking ($p<.04$, and .03, respectively). Education alone (Back School I) may have impact on perceived pain in General CLBP. PTSD may have a negative influence on outcomes in OEF/OIF Veterans with CLBP.					
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Introduction

Caused by exposure to trauma, post-traumatic stress disorder (PTSD) is a condition characterized by debilitating fear and anxiety. Of the spectrum of post-deployment mental disorders in Operation Enduring and Iraqi Freedom veterans (OEF/OIF; N = 73,157), PTSD was the highest in rate at 46% (VHA Office of Public Health and Environmental Hazards, November 2006). PTSD frequently co-occurs with other conditions, including chronic pain (Asmundson, Coons, Taylor & Katz, 2002; Asmundson & Hadjistavropolous, 2006; Asmundson & Taylor, 2006); in fact, there is evidence that suggests individuals with chronic pain may be particularly vulnerable to developing PTSD (Asmundson, Bonin, Frombach, & Norton, 2000).

Recent Veterans are displaying very high rates of comorbid pain conditions and PTSD (Clark, Bair, Buckenmaier, Gironde & Walker, 2007; Seal, Bertenthal, Miner, Sen & Marmar, 2007). Possibly due to the stigma associated with psychiatric care, many of these OEF/OIF Veterans are presenting in pain clinics instead of mental health settings (DeCarvalho & Whealin, 2006). Indeed, the prevalence of pain is high in OEF/OIF Veterans (Gironde, Clark, Massengale & Walker, 2006), and the most common complaint of this group is musculoskeletal pain with back pain as the most common site (41%; Cohen, Griffith, Larkin, Villena & Larkin, 2005).

The pain experience of the OEF/OIF Veteran population with PTSD is different than the conventional etiology of back pain. It has been observed clinically that individuals with PTSD are often challenged by psychological barriers to back pain treatment, and the literature suggests that pain-related fear and avoidance behavior may contribute to the development and maintenance of chronic pain. More specifically, research suggests that a fear of movement/(re)injury (i.e., "kinesiophobia") predicts pain-related avoidance behavior (i.e., poor treatment compliance) and subsequent disability (i.e., poor outcome) in patients with chronic pain (Reneman, Jorritsma, Dijkstra & Dijkstra, 2003; Vlaeyen, Kole-Snijders, Boeren & van Eek, 1995). Alternatively, it has been suggested that it is not the fear of pain that motivates avoidance behavior, but instead, the beliefs and cognitions about performing certain movements (e.g., "pain catastrophizing"; Kronshage, Kroener-Herwig & Pfingsten, 2001). Patients with PTSD and chronic low back pain (CLBP) clinically appear to carry beliefs that pain is a signal of serious damage to the body, making them vulnerable to the effects of catastrophizing, which has been defined as "an exaggerated negative orientation toward actual or anticipated pain experiences" (Gatchel, Peng, Peters, Fuchs & Turk, 2007, p. 602) and is a major aspect of fear-avoidance models of chronic pain (Asmundson, Norton, & Vlaeyen, 2004; Vlaeyen & Linton, 2000). Post-traumatic stress disorder (PTSD) is an anxiety disorder characterized by hypervigilance, reexperiencings and avoidance (American Psychological Association, 2000), likely increasing the susceptibility of a patient to such fears or cognitions, and hindering treatment. This is likely particularly true for patients whose pain is the result of trauma.

While "Back School" (i.e., education and lumbar stabilization exercises) is well-established as the standard clinical intervention for back pain, no studies have examined whether or not this intervention is effective for Veterans with CLBP and a significant comorbidity of PTSD. This is particularly concerning in the OEF/OIF Veteran population given their differences in demographics and etiology (Cohen et al., 2005). Clinical observation suggests the need for change to meet the unique needs of this population, and there is a clear "need for empirical data regarding trauma-related pain care" (Clark et al., 2007).

The purpose of the proposed research is to empirically explore the effectiveness of a standard clinical intervention, lumbar stabilization exercises ("Back School"), in Veterans with CLBP and PTSD in the areas of pain severity, perceived disability, and compliance and to likewise examine the prevalence of PTSD in those Veterans with CLBP. Specifically, it was expected that there would be high rates of PTSD in the population of CLBP patients referred to "Back School". It was further expected that

patients with PTSD would be found to have displayed less compliance with the “Back School” treatment program, express higher subjective levels of pain severity, and higher levels of perceived disability prior to intervention as compared to those veterans with CLBP only. The extent to which this was true in OEF/OIF Veterans was of particular interest.

Body

METHODS:

Participants. Approval was obtained from the local Institutional Review Board and the USAMRMC Office of Research Protections, Human Research Protection Office (HRPO). The proposed research is a pilot study using archival data over an 18 month period to examine the differential treatment outcomes of groups of military Veterans referred for a therapeutic exercise and education program, a standard clinical intervention for back pain ("Back School"). Inclusion criteria were: Veteran receiving care in the Veterans Affairs Health System, prior enrollment in Back School (2006-2007), diagnosis of chronic low back pain (CLBP) with a duration of 3 months or greater, documentation by physiatrist that spine is cleared for active therapies in Back School, and documented diagnosis of PTSD by a mental health provider. Exclusion criteria were: current enrollment in Back School (patient data must have been collected prior to the start of the study) and, therefore, patients were excluded if they underwent Back School beyond 2007, diagnosis of acute LBP (<3 months duration or less), PTSD not recorded as a diagnosis if no verification by mental health provider.

Intervention. The therapeutic exercise and education program for low back pain, "Back School," consists of two parts. Back School Part I is an educational component that introduces basic back anatomy and related musculature, correct body mechanics, postures, and simple back stretching and strengthening exercises which consists of one two-hour group class. Back School Part II, "Lumbar Stabilization Workshops," has fewer patients and consists of lumbar stabilization exercises. Only those patients who are capable of progressing to a more advanced exercise program are allowed to advance to this second portion. Patients must be deemed flexible enough to perform exercises in a prone or hand and knees position, motivated to learn, and committed to eight one-hour sessions over a period of one month. The second component of lumbar stabilization consists of an intermediate program to train the abdominal musculature to control the position of the pelvis. Patients must have flexibility to perform exercises and learn to bend from the hips instead of the lumbar spine. The exercises in the program progress from easier to more difficult postures (supine to prone to hands and knees to standing positions) and finally integrate functional activities of daily living. As part of the standard clinical component, patients are routinely asked to complete a standard clinical Back School Questionnaire prior to and after each of the two components of Back School.

Measures. Outcome measurements included: Visual Numeric Scale (VNS; Ritter, González, Laurent & Lorig, 2006), self-perceived disability (sit, walk), and compliance (attendance). Summary statistics (mean, standard deviation and frequency distribution) were generated for the baseline demographic information to characterize the subjects in the study.

RESULTS:

An initial 321 subjects were gathered from the Back School Log over 18 months and subsequently 318 charts were divided into four groups based on the diagnosis of PTSD and OEF/OIF status: Non-OEF/OIF Veterans without PTSD (Group 1), Non-OEF/OIF Veterans with PTSD (Group 2), OEF/OIF Veterans without PTSD (Group 3), and OEF/OIF Veterans with PTSD (Group 4). Three charts contained no other information than a sign-in and were ineligible for inclusion. ANOVA was used to compare continuous variables between groups and Chi Square or Fisher's Exact tests was used to compare categorical variables. All tests are two-sided and a p-value less than 0.05 was considered statistical significant. If there is statistical significant difference between the groups, subsequent analyses (2 sample t-test to compare continuous variables and Chi square test or Fisher's exact test to compare categorical variables) were done to compare various pair-wise groups or group combinations.

The mean age overall at participation in Back School was 55.86 years (SD = 13.88) with a significant difference ($p < .001$), between Non-OEF/OIF Groups 1 & 2 (59.34 years, SD = 11.4) and OEF/OIF Groups 3 & 4 (35.24 years, SD = 8.08). While males were the overall majority (95.6%), significantly more females (20%) constituted the OEF/OIF Groups 3 & 4 ($p < .001$). The vast majority of the subjects were African-American (46%) or Caucasian (46%). There was no difference among groups

in regard to race or marital status. [See Table 1.] The majority of those with PTSD were from the United States Army branch of service (65.28%, $p = .003$). Combat exposure was significantly increased in the OEF/OIF subjects (Groups 3 & 4) with 34.78% versus 17.6% exposed in the non-OEF/OIF Veterans (Groups 1 & 2), $p = .002$. [See Figure 1].

There was no significant difference among Veterans in their pre-intervention self-perceived pain with an overall mean VNS rating of 4.9. The majority of Veterans (310/318 subjects, 97.48%) completed Back School I (Education) without a difference in attendance among groups. However, there was a significant improvement in VNS score ($p = .002$) in those subjects without a diagnosis of PTSD in Groups 1 and 3. [See Figure 2].

There was no difference in the self-reported ability to sit or walk post-Back School I intervention. Of those who continued on to Back School II Lumbar Stabilization Workshops (119/318, 37.5%), 113 of 119 had available data for review. There was a difference in attendance among groups with 101 of 113 subjects (89.39%) completing Back School II. Specifically, there was only a 50% completion rate in Group 4, OEF/OIF Veterans with PTSD, $p=0.049$. [See Figure 3].

At baseline, the average pre-Back School II VNS score showed no difference among groups and there was no significant difference in the change of self-perceived pain score post Back School II. However, there was a significant difference in self-reported function. The OEF/OIF Veterans regardless of PTSD status (both Groups 3 & 4) demonstrated a lower change of improvement with self-reported sitting post-intervention ($p = .042$). Those with a diagnosis of PTSD in Groups 2 & 4 also showed a lower change of improvement with self-reported ability to walk ($p = .033$). [See Figures 4 and 5].

CONCLUSION

Education alone (i.e. in Back School), may have a positive impact on perceived pain in those patients with a diagnosis of CLBP. However, the comorbid diagnosis of PTSD in those with CLBP may have a negative influence on outcomes of pain, self-reported function, and compliance with prescribed therapeutic exercise with CLBP, especially in recently returning OEF/OIF Veterans.

DISCUSSION:

Results of this work have the potential to enhance existing knowledge of what contributes to poor treatment outcome in our OEF/OIF Veteran population with CLBP. Based on the results of this study, there are three main areas that need to be addressed in future studies in removing barriers to treatment: 1. increasing compliance, 2. treating the negative effects of PTSD or its components (anxiety, fear, kinesiophobia, or catastrophizing) that may be interfering with function, and 3. acknowledging and addressing effects of recent trauma in those returning OEF/OIF Veterans. This study confirms that even education alone about one's condition received in Back School I improves self-perceived severity of pain in those general subjects with CLBP without PTSD. While those with PTSD had similar levels of perceived pain at baseline, this did not improve with education alone. As expected, education alone did not change self-perceived function across all groups. What is striking about the overall groups, however, is that only 37% of Back School I participants went on to Back School II. There is an additional "silent majority" (63%) of those who have not been surveyed which makes the self-reported functional gains from Back School II difficult to generalize. And a significant percentage of OEF/OIF Veterans with PTSD (Group 4) had a higher rate of non-compliance than the other groups. In those that did participate, there were gains in perceived functional improvement in those Non-OEF/OIF Veterans (Group 1 & 2) in regards to sitting. Additionally, participation and compliance with lumbar stabilization exercise program demonstrated gains in perceived functional improvement in those without PTSD (Groups 1 & 3) in regards to walking.

These clinically and statistically significant self-reported functional gains from Back School II reinforce the need for a more nuanced approach to CLBP treatment with individuals recently exposed to trauma in especially with individuals with CLBP experiencing a comorbid mental health condition (i.e. PTSD). There is the potential development of efficacious wellness interventions that promote healing and focus on integration of mind and body after combat exposure in OEF/OIF Veterans. In addition,

there needs to be a development of interventions to decrease overall levels of disability in this population with a coexisting diagnosis of PTSD. Future studies can also provide an opportunity to examine cost-effectiveness of health care services.

This study had potential weaknesses due to its retrospective design. However, this allowed a historical perspective of those who have already been treated with a standardized intervention for chronic low back pain. The small cell sizes increase the chances of a Type II error, i.e. compliance. In addition, because only those patients with a confirmed diagnosis of PTSD were included in this study, the symptoms associated with PTSD may be under-recognized in these recently returning OEF/OIF Veterans. In addition, participants in Back School II may not be representative of the patients with CLBP. However, as the numbers of returning Veterans are increasing with the ongoing conflict, this allows for a future cohort clinical study that can address larger cell sizes for comparison, and an opportunity to increase retention in those progressing from Back School I to II in order to make a future study population more generalizable.

Any future directions should include a prospective study with complementary clinical interventions that can potentially address barriers to treatment: In addition, results from this study invite the addition of concurrent treatment to address compliance by addressing symptoms of PTSD and recent trauma in addition to standardized clinical intervention in those with CLBP and PTSD. A prospective trial would be advantageous to have standardized outcome measures and explore complementary options. Information gathered from this pilot trial will potentially enhance awareness of the need for a more innovative and transdisciplinary approach to the treatment of CLBP in Veterans with comorbid PTSD that can eventually be empirically tested through clinical trial research.

Key Research Accomplishments

- A poster was presented to the sponsoring agency by invitation at the Military Health Conference, Kansas City, MO September 1, 2009. Poster: Wallbom AS, T Victor, A Miranda, et al. A pilot study to identify barriers to treatment in OEF/OIF Veterans with post-traumatic stress disorder and low back pain. Military Health Conference 2009. Kansas City, Missouri, 1 September 2009.
- Manuscript preparation is in progress.
- Future application for additional funding based on this work is in progress.

Reportable Outcomes

A poster was presented to the sponsoring agency by invitation at the Military Health Conference, Kansas City, MO September 1, 2009. Poster: Wallbom AS, T Victor, A Miranda, et al. A pilot study to identify barriers to treatment in OEF/OIF Veterans with post-traumatic stress disorder and low back pain. Military Health Conference 2009. Kansas City, Missouri, 1 September 2009.

Conclusion

Education alone (i.e. in Back School I), may have a positive impact on perceived pain in those patients with a diagnosis of CLBP. However, the comorbid diagnosis of PTSD in those with CLBP may have a negative influence on outcomes of pain, self-reported function, and compliance with prescribed therapeutic exercise with CLBP, especially in recently returning OEF/OIF Veterans.

References

- American Psychiatric Association. (2000). *Diagnostic and statistical manual of mental disorders* (4th ed.), text revision (DSM-IV-TR). Washington, D.C.: Author.
- Asmundson, G. J. G., Bonin, M. F., Frombach, I. K., & Norton, G. R. (2000). Evidence of a disposition toward Tearfulness and vulnerability to posttraumatic stress in dysfunctional pain patients. *Behaviour Research & Therapy*, 38, 801-812.
- Asmundson, J.G.G., Coons, M.J., Taylor, S. & Katz, J. (2002). PTSD and the experience of pain: Research and clinical implications of shared vulnerability and mutual maintenance models. *Canadian Journal of Psychiatry*, 47, 930-937.
- Asmundson, G.J.G. & Hadjistavropoulos, H.D. (2006). Addressing shared vulnerability for comorbid PTSD and chronic pain: A cognitive-behavioral perspective. *Cognitive and Behavioral Practice*, 13, 8-16.
- Asmundson, J.G.G. & Taylor, S. (2006). PTSD and chronic pain: Cognitive-behavioral perspectives and practical implications. In G. Young, A.W. Kane & K. Nicholson (Eds.), *Psychological knowledge in court: PTSD, pain and TBI*. New York, NY: Springer.
- Asmundson, G.J.G., Norton, P.J. & Vlaeyen, J.W.S. (2004). Fear-avoidance models of chronic pain: An overview. In G.J.G. Asmundson, J.W.S. Vlaeyen & G. Crombez (Eds.), *Understanding and treating fear of pain*. Oxford, England: Oxford University Press.
- Clark, M.E., Bair, M.J., Buckenmaier, C.C., Gironde, R.J. & Walker, R.L. (2007). Pain and combat injuries in soldiers returning from Operations Enduring Freedom and Iraqi Freedom: Implications for research and practice. *Journal of Rehabilitation Research and Development*, 44, 179-194.
- Cohen, S.P., Griffith, M.S., Larkin, T.M., Villena, F. & Larkin, R. (2005). Presentation, diagnosis, mechanisms of injury, and treatment of soldiers injured in Operation Iraqi Freedom: An Epidemiological study conducted at two military pain management centers. *Anesthesia Analgesics*, 101, 1098-1103.
- DeCarvalho, L.T. & Whealin, J.M. (2006). What pain specialists need to know about posttraumatic stress disorder in Operation Iraqi Freedom and Operation Enduring Freedom Returnees. *Journal of Musculoskeletal Pain*, 14, 37-45.
- Gatchel, R.J., Peng, Y.B., Peters, M.L., Fuchs, P.N. & Turk, D.C. (2007). The biopsychosocial approach to chronic pain: Scientific advances and future directions. *Psychological Bulletin*, 133, 581-624.
- Gironde, R.J., Clark, M.E., Massengale, J.P. & Walker, R. (2006). Pain among Veterans of Operations Enduring Freedom and Iraqi Freedom. *Pain Medicine*, 7, 339-343.
- Kronshage, U., Kroener-Herwig, B. & Pflingsten, M. (2001). Kinesiophobia in chronic low back pain patients-Does the startle paradigm support the hypothesis? *International Journal of Behavioral Medicine*, 8, 304-318.
- Reneman, M.F., Jorritsma, W., Dijkstra, S.J. & Dijkstra, P.U. (2003). Relationship between kinesiophobia and performance in a functional capacity evaluation. *Journal of Occupational Rehabilitation*, 13, 277-284.

Ritter, P.L., González, V.M., Laurent, D.D., Lorig, K.R. (2006). Measurement of Pain Using the Visual Numeric Scale. *Journal of Rheumatology*, 33, 574-580.

Seal, K.H., Bertenthal, D., Miner, C.R., Sen, S. & Marmar, C. (2007). Bringing the war back home. *Archives of Internal Medicine*, 167, 476-482.

VHA Office of Public Health and Environmental Hazards. (November 2006). Accessible at <http://www.publichealth.va.gov/>.

Vlaeyen, G., Kole-Snijders, A. M. J., Boeren, R. G. B., & van Eek, H. (1995). Fear of movement/(re)injury in chronic low back pain and its relation to behavioral performance. *Pain*, 62, 363–372.

Vlaeyen, G. & Linton, S.J. (2000). Fear-avoidance and its consequences in chronic musculoskeletal pain: A state of the art. *Pain*, 85, 317-332.

Appendices

Table 1. Sample demographics in four groups of Veterans.

Characteristic	Overall n = 318	Group 1 n = 213	Group 2 n = 59	Group 3 n = 33	Group 4 n = 13	Test of significance
Age (in years) Mean (SD)	55.86 (13.9)	55.86 (13.9)	55.86 (13.9)	55.86 (13.9)	55.86 (13.9)	p<.0001
Gender % Male	96%	98%	98%	76%	92%	p<.0001
Race % Black Caucasian	46% 46%	47% 49%	57% 35%	23% 47%	42% 42%	Ns
Marital Status % Single Divorced Married	37% 30% 24%	38% 31% 22%	39% 15% 32%	21% 45% 30%	38% 38% 15%	Ns

Figure 1. Exposure to combat reported by four groups of Veterans.

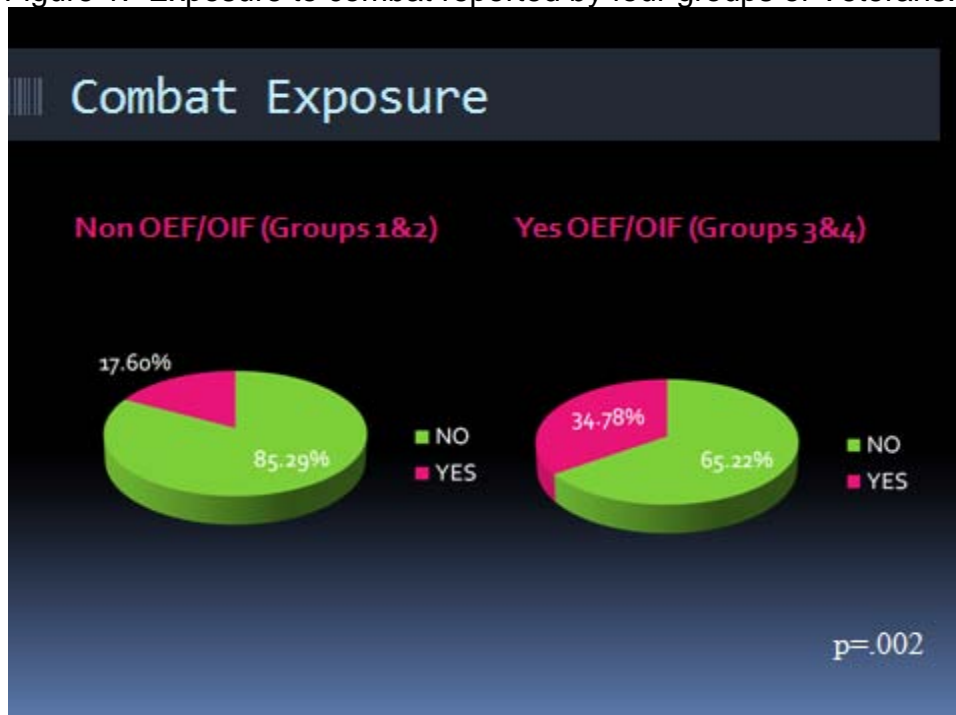


Figure 2. Contrasting Visual Numeric Scale values after Back School I for PTSD groups.

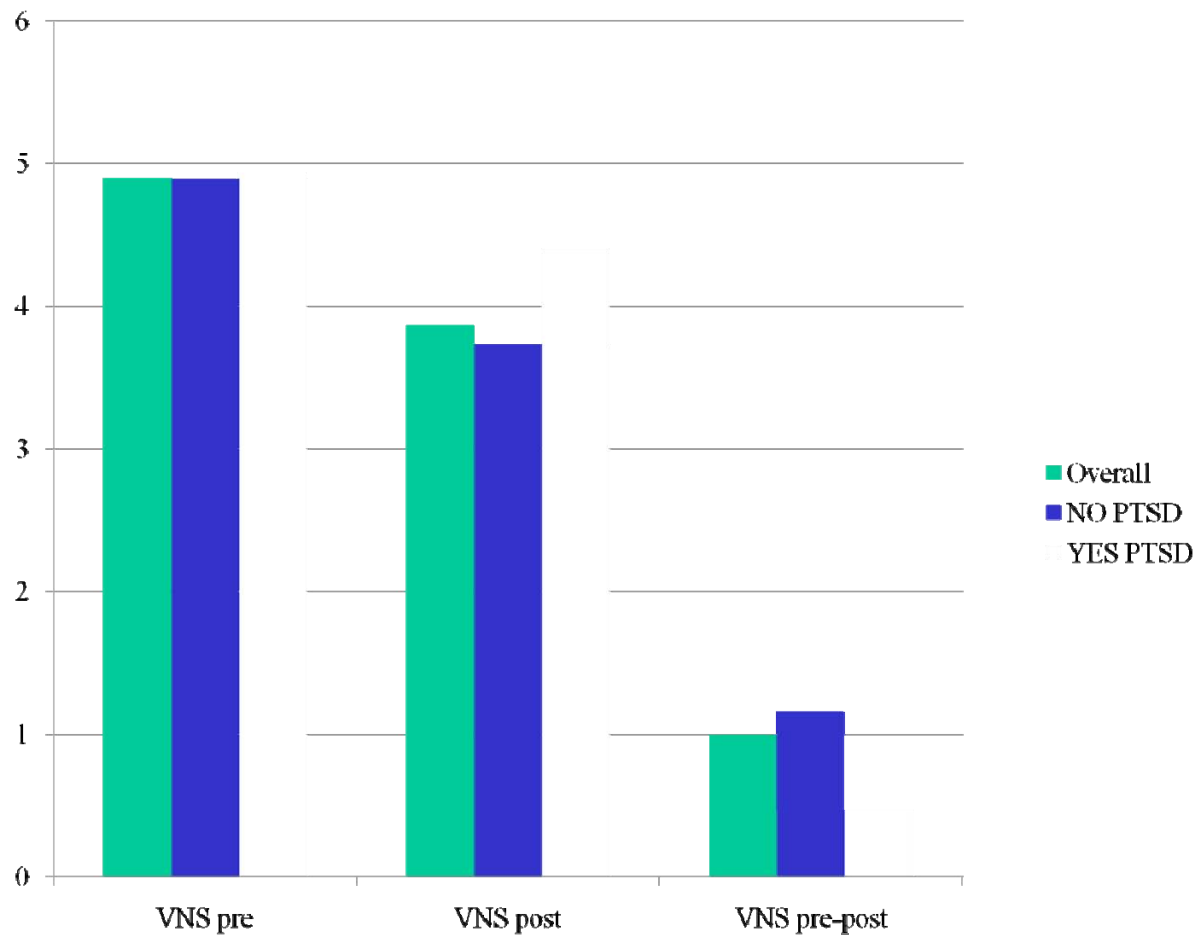


Figure 3. Back School II Completion Rate for four groups.

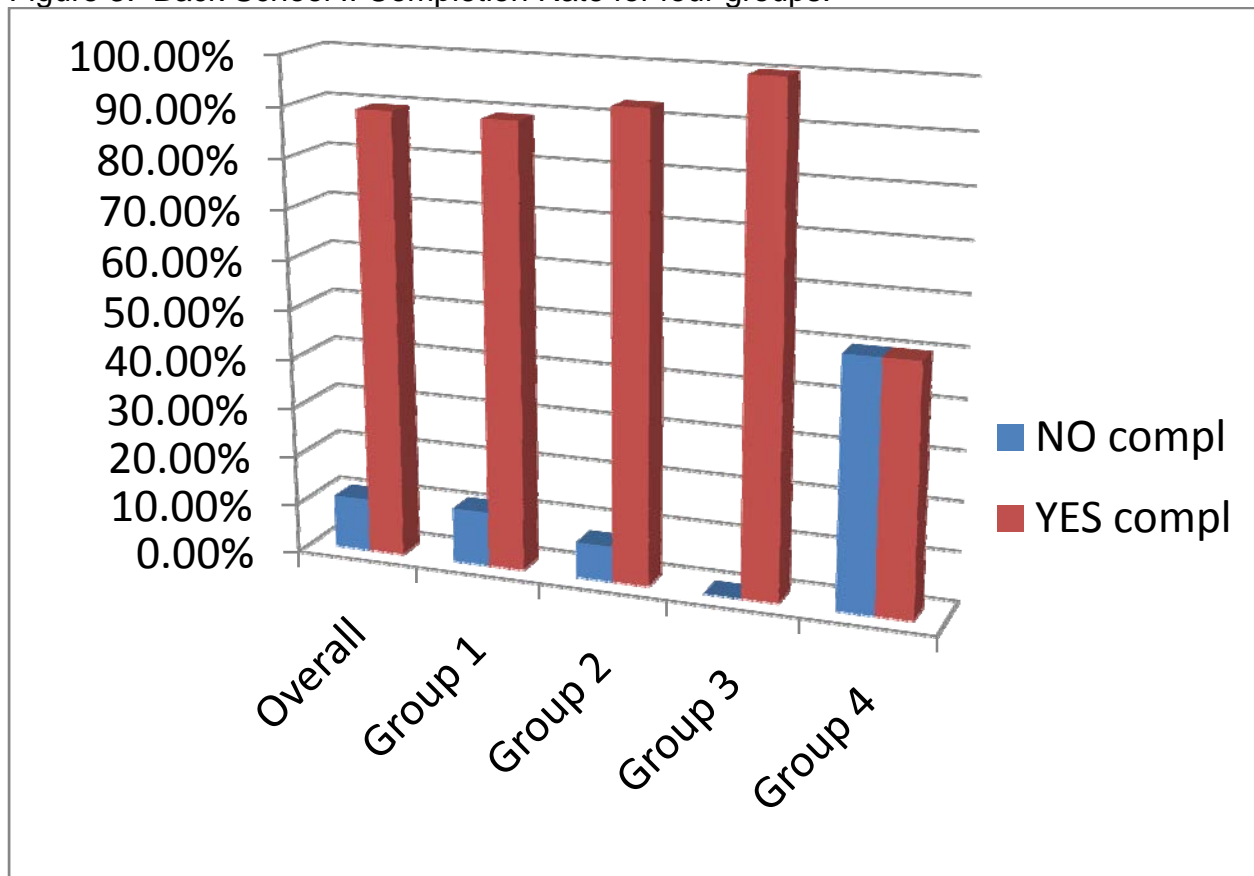
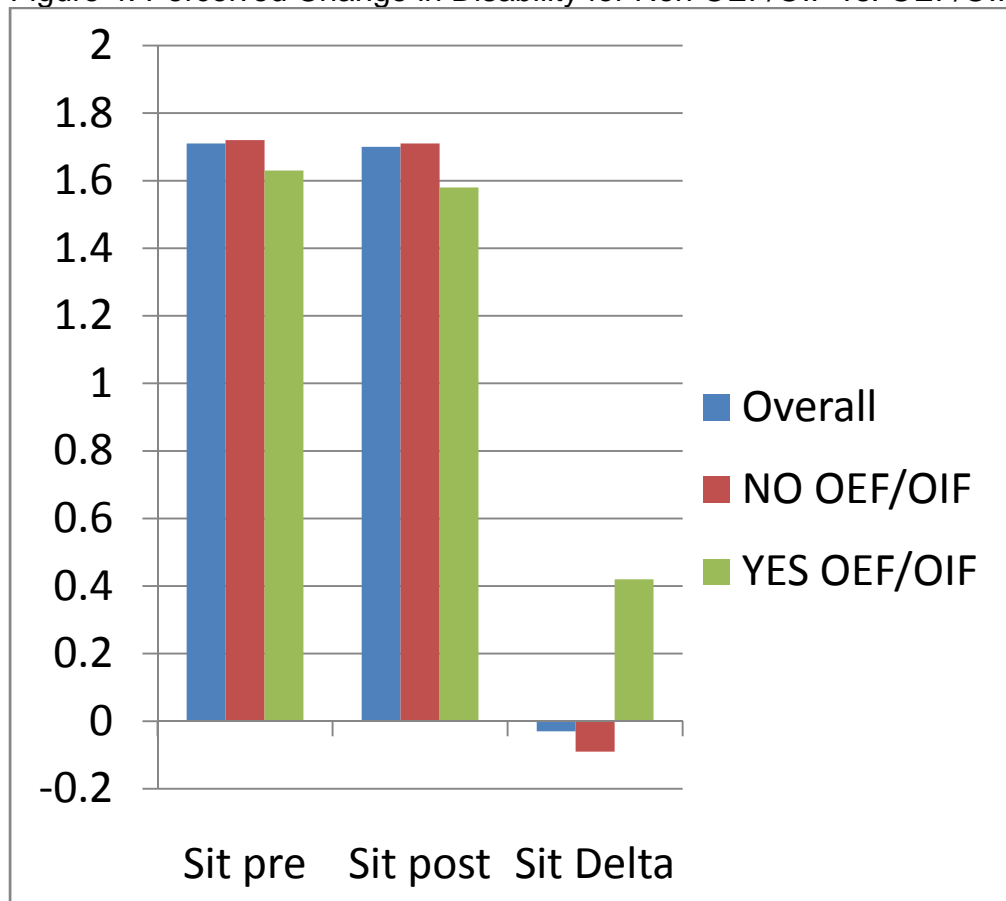
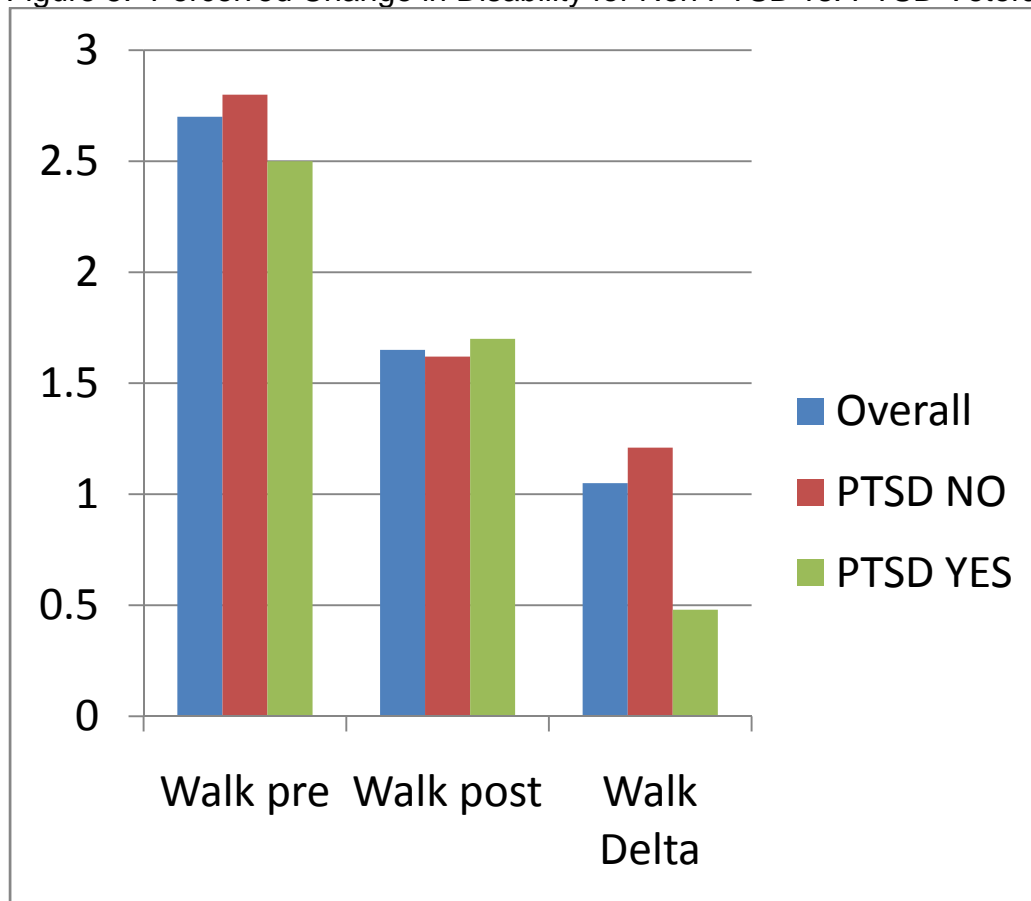


Figure 4. Perceived Change in Disability for Non OEF/OIF vs. OEF/OIF Veterans.



Note: Negative Delta indicates improvement; positive Delta indicates decreased function.

Figure 5. Perceived Change in Disability for Non PTSD vs. PTSD Veterans.



Note: Positive Delta indicates improved function.